

## The role of hematological parameters in the diagnosis of hyperemesis gravidarum

Hematological parameters in hyperemesis gravidarum

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### Abstract

**Aim:** Various factors play a role in the development of hyperemesis. The role of inflammation in the development of hyperemesis gravidarum has not been elucidated. In our study, it was aimed to analyze the changes in some hematological parameters and inflammatory indicators and possible relationships of these parameters with each other in patients with hyperemesis gravidarum.

**Materials and Methods:** The study included 87 patients diagnosed with hyperemesis and 24 controls admitted to our hospital between April 1, 2018 and October 1, 2018. Prospectively, blood samples were taken from all patients, and complete blood tests were performed.

**Results:** The mean age of the patients included in the study was  $25.4 \pm 5.0$  years (age range: 17-39 years). The mean platelet distribution (PDW) in the hyperemesis group ( $14.7 \pm 2.3$ ) was significantly lower than the control group ( $p=0.007$ ). No significant differences were found between the hyperemesis group and the controls in terms of mean blood leukocyte ( $p=0.146$ ), neutrophil ( $p=0.266$ ), lymphocyte ( $p=0.778$ ), hemoglobin ( $p=0.787$ ), hematocrit ( $p=0.223$ ), platelet ( $p=0.447$ ), mean platelet volume ( $p=0.443$ ), CRP ( $p=0.91$ ), neutrophil/lymphocyte ratio ( $p=0.207$ ) and platelet/lymphocyte ratio ( $p=0.237$ ). There was a significant correlation between the neutrophil/lymphocyte ratio and leukocyte levels in the hyperemesis group ( $p=0.001$ ).

**Discussion:** In conclusion, our study shows that inflammatory indicators such as neutrophil/lymphocyte and platelet/lymphocyte ratios, leukocyte count, and CRP levels cannot be directly associated with the hyperemesis gravidarum manifestation.

### Keywords

Hyperemesis Gravidarum; Neutrophil/Lymphocyte Ratio, Platelet/Lymphocyte Ratio

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## Introduction

Nausea and vomiting complaints are very common during pregnancy. Up to 90% of pregnant women experience nausea in the early period. It has been reported that nausea during pregnancy is caused by an increase in the level of human chorionic gonadotropin hormone (HCG) [1-3]. Hyperemesis gravidarum is a clinical manifestation characterized by increased severity and duration of nausea and vomiting. Nutritional disorders, dehydration, electrolyte disorders, weight loss, and ketonuria can also be added to the picture, which may worsen the clinical course of the pregnant woman. Hyperemesis gravidarum, which can develop in almost 2% of pregnant women, may be at a level that may require hospitalization in some patients [1-5].

A wide variety of factors play a role in the development of hyperemesis gravidarum. These include increased beta-HCG level, steroids, multiple pregnancy, increased body mass index, and a history of hyperemesis gravidarum, but the exact cause of the hyperemesis has not been elucidated [3-5]. Serious complications can also be developed in some pregnant women with hyperemesis gravidarum such as Wernicke encephalopathy and thromboembolism, preterm birth, low birth weight, retarded growth, some congenital anomalies, and fetal death. Therefore, it is necessary to closely monitor the hyperemesis gravidarum, and it is important to provide supportive treatment to these pregnant women quickly [3-7].

In chronic inflammation, proliferation is observed in the megakaryocytic series, which leads to the emergence of relative thrombocytosis. In this picture, the lymphocyte count decreases due to severe apoptosis. Platelets have been reported to play a role in regulating inflammatory reactions as well as coagulation and hemostasis. For this reason, it has been reported that the platelet/lymphocyte ratio is associated with some inflammatory diseases [8-9]. Likewise, the neutrophil/lymphocyte ratio and platelet distribution width (PDW) levels have been shown to change in some inflammatory conditions. It has been reported that there is a significant relationship between hyperemesis gravidarum and platelet/lymphocyte and neutrophil/lymphocyte ratios and some other inflammatory indicators [9-12].

In the present study, it was aimed to analyze the changes in some hematological parameters and inflammatory indicators and possible relationships of these parameters with each other in patients with hyperemesis gravidarum.

## Material and Methods

### Patients and Tests

The study group included 87 patients diagnosed with hyperemesis gravidarum between the ages of 17 and 39 who admitted to the gynecology outpatient clinics of our hospital between April 1, 2018 and October 1, 2018 and 24 pregnant women without hyperemesis. Participants have provided voluntary informed consent before the study. Pregnant women with single live pregnancy accompanied by ketosis accompanied by recurrent nausea, vomiting, and dehydration findings were also accepted. Pregnant women with additional systemic disease, signs of infection, those with a pre-diagnosis of abortion imminens, those with fetal congenital malformation,

and smokers were not included in the study. The gestational age of the patients was determined using the first day of the last menstrual period, and was confirmed by ultrasonography. Prospectively, all patients' peripheral venous blood samples were taken from the antecubital vein at the time of admission, and were examined in the laboratory within 1 hour. Laboratory parameters including complete blood count, C-reactive protein (CRP) of all participants were recorded. Blood samples were taken into standard tubes containing dipotassium ethylenedinitro tetraacetic acid (EDTA) for complete blood count (CBC) using the Coulter LH 780 device (Beckman Coulter, Brea, CA, USA). Leukocyte, neutrophil, lymphocyte, hemoglobin, hematocrit, platelet, mean platelet volume (MPV), mean platelet distribution (PDW), CRP, neutrophil/lymphocyte ratio and platelet/lymphocyte ratio were recorded as hematological parameters. The neutrophil/lymphocyte ratio (NLR) was divided by the number of neutrophils from the blood parameters to the number of lymphocytes; platelet/lymphocyte ratio (PLR) was obtained by dividing the number of platelets into the number of lymphocytes. This study was approved by the local ethics committee and was planned prospectively.

### Statistical analysis

All statistical analyzes in the study were done using SPSS 25.0 software (IBM SPSS, Chicago, IL, USA). Descriptive data are given as numbers and percentages. In terms of categorical variables, comparisons between groups were made with the Pearson's Chi-Square test and the Fisher's Exact test. Whether continuous variables are suitable for normal distribution was confirmed by the Kolmogorov-Smirnov test. The differences between the groups in terms of continuous variables were made using the Student's t-test and the comparison of mean values between multiple groups by variance analysis. The relationship between continuous variables was tested with the Spearman's correlation analysis. The results were evaluated within the 95% confidence interval and  $p < 0.05$  values were considered significant. Bonferroni correction was made where appropriate.

## Results

The mean age of the patients included in the study was  $25.4 \pm 5.0$  years (age range: 17-39 years). The mean gestational week was  $10.3 \pm 4.0$  weeks (range: 4-27 weeks). There was no significant difference between the groups in terms of mean age ( $p=0.194$ ) and mean gestational week ( $p=0.082$ ).

When blood parameters were evaluated, PDW percentage ( $14.7 \pm 2.3$ ) in the hyperemesis group was significantly lower than the control group ( $16.0 \pm 0.5$ ) ( $p=0.007$ ). There was no significant difference in the mean blood leukocyte ( $p=0.146$ ), neutrophil ( $p=0.266$ ), lymphocyte ( $p=0.778$ ), hemoglobin ( $p=0.787$ ), hematocrit ( $p=0.223$ ), platelet ( $p=0.447$ ), mean platelet volume ( $p=0.443$ ), CRP ( $p=0.91$ ), neutrophil/lymphocyte ( $p=0.207$ ) and platelet/lymphocyte ratios ( $p=0.237$ ) between the hyperemesis group and the control group (Table 1).

A significant correlation was found between the neutrophil/lymphocyte ratio and leukocyte levels in the hyperemesis group ( $p=0.001$ ,  $r=0.339$ ) (Table 2).

**Table 1.** Comparison of mean values of hematologic parameters by groups

	Hyperemesis group		Controls	
	Mean	SD	Mean	SS
Leukocyte (103/mL)	8.2	2.2	7.5	1.8
Neutrophil (mg/dL)	5.3	1.8	4.9	1.6
Neutrophil (%)	67.3	7.2	65.1	7.8
Lymphocyte (103/mL)	1.9	0.5	1.9	0.4
Lymphocyte (%)	24.4	7.1	25.6	8.0
Hemoglobin (g/dL)	12.5	0.9	12.5	1.1
Hematocrit (%)	37.2	2.8	38.0	3.4
Platelet (103/mL)	242.5	50.3	233.5	54.3
MPV (fL)	9.1	1.1	8.9	1.0
PDW (%)	14.7	2.3	16.0	0.5
RDW (%)	12.9	1.2	13.4	1.2
CRP (mg/L)	1.4	2.0	1.4	2.2
Neutrophil/Lymphocyte ratio	3.1	1.5	2.7	1.0
Platelet/Lymphocyte ratio	139.2	50.0	126.2	37.0

SD: Standard deviation, MPV: Mean platelet volume, PDW: Platelet distribution width RDW: Erythrocyte distribution width, CRP: C-reactive protein.

**Table 2.** Association of neutrophil/lymphocyte and platelet/lymphocyte ratios with C-reactive protein and leukocyte counts in the hyperemesis group

	CRP level		Leukocyte count
	r	p	r
Neutrophil/Lymphocyte ratio	-0.002	0.987	0.339
Platelet/Lymphocyte ratio	0.061	0.577	-0.167

CRP: C-reactive protein.

## Discussion

Changes in the number or rates of inflammatory indicators in the bloodstream such as leukocyte, neutrophil, lymphocyte, platelet, and CRP are observed during inflammation. These inflammatory indicators have been associated with many acute or chronic diseases and can be used predictively in the early diagnosis of some diseases, in some cases in the diagnosis and in the follow-up of the treatment or clinical picture [9-12]. Hyperemesis gravidarum is a clinical manifestation that can develop due to many hormonal, psychosocial or biochemical factors [1, 2]. An alteration can be observed in these indicator levels in pregnant women with hyperemesis table [9,11,12].

The role of inflammation in the development of hyperemesis gravidarum has not been elucidated [11]. Engin-Üstün et al. [12] reported a significant increase in CRP level in pregnant women with hyperemesis gravidarum. Kan et al. [13] found that the mean neutrophil and platelet counts increased significantly in the hyperemesis group compared to the control group. Butcher [14] reported in his study that there was no significant difference between pregnant women diagnosed with hyperemesis and the control group in terms of mean leukocyte count, platelet count, and hemoglobin level. In our study, no significant difference was found between hyperemesis and control groups in terms of mean leukocyte, neutrophil, lymphocyte, hemoglobin, hematocrit, platelet, mean platelet volume and CRP. These data

show that hematological parameters do not alter in pregnant women with hyperemesis compared to normal pregnant, and that blood parameters do not provide reliable data in predicting the presence of hyperemesis.

It has been reported that neutrophil/lymphocyte and platelet/lymphocyte ratios may increase in inflammatory conditions [11]. Beyazit et al. [11] found that neutrophil/lymphocyte and platelet/lymphocyte ratios were significantly increased in hyperemesis gravidarum patients. However, they did not specifically attribute this to hyperemesis, and they concluded that these high rates were due to an increase in neutrophil count and a decrease in lymphocyte count in the bloodstream as a result of an immune response to hyperemesis-related physical stress. In addition, Kurt et al. [15] and Çağlayan et al. [16] reported that neutrophil/lymphocyte and platelet/lymphocyte ratios were significantly increased in hyperemesis patients. Kan et al. [13] reported that neutrophil/lymphocyte and platelet/lymphocyte ratios were significantly increased in the hyperemesis group, but they could not find a threshold value with high sensitivity and specificity ratios for these ratios by ROC analysis. Likewise, Tayfur et al. [9] also reported that neutrophil/lymphocyte and platelet/lymphocyte ratios were significantly higher in the hyperemesis group, but these researchers did not find reliable threshold values for hyperemesis detection with their ROC analysis. In our study, no significant difference was found between hyperemesis and control groups in terms of neutrophil/lymphocyte and platelet/lymphocyte ratios. These data show that neutrophil/lymphocyte and platelet/lymphocyte rates increase in inflammation but these ratios cannot be directly related to hyperemesis.

Beyazit et al. [11] reported a significant correlation between neutrophil/lymphocyte ratio and CRP level in pregnant women with hyperemesis, but they could not find the same relationship between platelet/lymphocyte ratios and CRP. These researchers also reported that there was no significant correlation between neutrophil/lymphocyte and platelet/lymphocyte ratios and leukocyte count [11]. In our study, no correlation was found between the neutrophil/lymphocyte and platelet/lymphocyte ratios and CRP and leukocyte levels in the hyperemesis group. These data show that although there may be an alteration in neutrophil and CRP levels in the case of inflammation, these alterations are not directly related to the hyperemesis table.

It is known that PDW value, which is the platelet distribution width, is an indicator of platelet function and activation. PDW level has been reported to increase in some chronic disorders such as diabetes, cancer, cardiological and respiratory diseases. Moreover, increased PDW level has been shown to be informative for prognosis in some patients [8,17]. However, there is insufficient data regarding the possible relationship between hyperemesis gravidarum and PDW levels. Beyazit et al. [11] found no significant difference in terms of PDW level between hyperemesis and control groups. Çintesun et al. [18] also found similar PDW levels among the groups. In our study, the mean PDW level in hyperemesis patients decreased significantly compared to the control group. These findings show that PDW value may not provide reliable data in the diagnosis or follow-up of hyperemesis.

There were some limitations in our study. Since our research was a cross-sectional study, pregnant women were not monitored

in terms of alterations in the inflammatory indicators during or after pregnancy. In our study, since the hyperemesis level was not classified, it could not be analyzed whether the factors examined had an effect on the hyperemesis level.

### Conclusion

In conclusion, our study shows that inflammatory indicators such as neutrophil/lymphocyte and platelet/lymphocyte ratios, leukocyte count, and CRP levels cannot be directly associated with the hyperemesis gravidarum table. Larger-scale clinical studies should be conducted to further evaluate the diagnostic and prognostic significance of these hematological markers in hyperemesis patients.

### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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### Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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